



03C0

Box  
Seq

PATENT

Docket No. DIV-1460-21US (112766-199)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of: Short et al. Confirmation No. 4125  
U.S. Serial No.: 10/029,221  
Filing Date: December 21, 2001  
Title: EXONUCLEASE-MEDIATED NUCLEIC ACID REASSEMBLY IN  
DIRECTED EVOLUTIONS

**Hand Carried directly to Customer Window at:**  
2011 South Clark Place  
Crystal Plaza Two, Lobby, Room 1B03, Box Sequence  
Arlington, VA 22202

**COMMUNICATION IN REPLY TO NOVEMBER 29, 2002 NOTICE TO COMPLY WITH  
REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE  
SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES**

Dear Commissioner:

This Communication is submitted in reply to the Notice mailed November 29, 2002 in connection with the above-identified application. A reply is due January 29, 2003. Therefore, this Communication is being timely filed.

In response to the Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures mailed by the United States Patent and Trademark Office on November 29, 2002, applicant submits the following documents for filing in the above-referenced patent application:

1. A copy of the Notice Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures mailed on November 29, 2002;
2. Statement Under 37 C.F.R. § 1.821-1.825;
3. Diskette Containing Computer Readable Format of Sequence Listing;
4. Paper copy of the Sequence Listing; and

Applicants: Jay M. Short et al.  
U.S. Serial No.: 10/029,221  
Filed: December 21, 2001  
Page 2

5. Return Postcard.

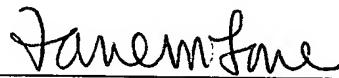
No fees are believed to be due in connection with this letter. However, please charge any additional costs or credit any overpayment to maintain the pendency of this application to our Deposit Account No. 08-0219.

If there are any questions, please call the undersigned at the telephone number indicated below.

Date: \_\_\_\_\_

1/9/03

Respectfully submitted,



Jane M. Love, Ph.D.  
Registration No. 42,812  
Attorney for Applicants

Hale and Dorr LLP  
300 Park Avenue  
New York, NY 10022  
Tel. (212) 937-7233  
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UNITED STATES  
PATENT AND  
TRADEMARK OFFICE

REC'D DEC 03 2002

Commissioner for Patents  
Washington, DC 20231  
www.uspto.gov

APPLICATION NUMBER	FILING/RECEIPT DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NUMBER
10/029,221	12/21/2001	Jay M. Short	DIV-1460-21US (112766-199

CONFIRMATION NO. 4125

28089  
HALE AND DORR LLP  
300 PARK AVENUE  
NEW YORK, NY 10022

## FORMALITIES LETTER



\*OC000000009175999\*

Date Mailed: 11/29/2002

**NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS  
CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE  
DISCLOSURES**

Filing Date Granted

Applicant is given **TWO MONTHS FROM THE DATE OF THIS NOTICE** within which to file the items indicated below to avoid abandonment. Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

- A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing." Applicant must provide a substitute computer readable form (CRF) copy of the "Sequence Listing" and a statement that the content of the sequence listing information recorded in computer readable form is identical to the written (on paper or compact disc) sequence listing and, where applicable, includes no new matter, as required by 37 CFR 1.821(e), 1.821(f), 1.821(g), 1.825(b), or 1.825(d).

For questions regarding compliance to these requirements, please contact:

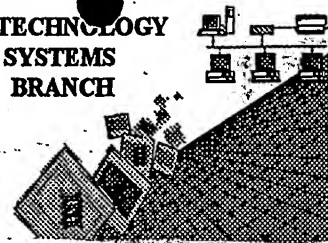
- For Rules Interpretation, call (703) 308-4216
- To Purchase PatentIn Software, call (703) 306-2600
- For PatentIn Software Program Help, call (703) 306-4119 or e-mail at [patin21help@uspto.gov](mailto:patin21help@uspto.gov) or [patin3help@uspto.gov](mailto:patin3help@uspto.gov)

*A copy of this notice **MUST** be returned with the reply.*

  
Customer Service Center

Initial Patent Examination Division (703) 308-1202

PART 1 - ATTORNEY/APPLICANT COPY



## **RAW SEQUENCE LISTING ERROR REPORT**

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: 10/029,221B  
Source: OIPF  
Date Processed by STIC: 11/6/02

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.

PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:

- 1) INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,
- 2) TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY

FOR CRF SUBMISSION QUESTIONS, PLEASE CONTACT MARK SPENCER, 703-308-4212.

FOR SEQUENCE RULES INTERPRETATION, PLEASE CONTACT ROBERT WAX, 703-308-4216.

PATENTIN 2.1 e-mail help: [patin21help@uspto.gov](mailto:patin21help@uspto.gov) or phone 703-306-4119 (R. Wax)

PATENTIN 3.0 e-mail help: [patin3help@uspto.gov](mailto:patin3help@uspto.gov) or phone 703-306-4119 (R. Wax)

TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE **CHECKER  
VERSION 3.1 PROGRAM**, ACCESSIBLE THROUGH THE U.S. PATENT AND  
TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:

**<http://www.uspto.gov/web/offices/pac/checker>**

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail.

Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.

Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

1. EFS-Bio (<<http://www.uspto.gov/ebc/efs/downloads/documents.htm>> , EFS Submission User Manual - ePAVE)
2. U.S. Postal Service: U.S. Patent and Trademark Office, Box Sequence, P.O. Box 2327, Arlington, VA 22202
3. Hand Carry directly to:  
U.S. Patent and Trademark Office, Technology Center 1600, Reception Area, 7<sup>th</sup> Floor, Examiner Name,  
Sequence Information, Crystal Mall One, 1911 South Clark Street, Arlington, VA 22202  
Or  
U.S. Patent and Trademark Office, Box Sequence, Customer Window, Lobby, Room 1B03, Crystal Plaza Two,  
2011 South Clark Place, Arlington, VA 22202
4. Federal Express, United Parcel Service, or other delivery service to: U.S. Patent and Trademark Office,  
Box Sequence, Room 1B03-Mailroom, Crystal Plaza Two, 2011 South Clark Place, Arlington, VA 22202

Revised 01/29/2002



Does Not Comply  
Corrected Diskette Needed

OIPE

Error on p. 3

RAW SEQUENCE LISTING  
PATENT APPLICATION: US/10/029,221B

DATE: 11/06/2002  
TIME: 14:55:15

Input Set : A:\112766-199.ST25.txt  
Output Set: N:\CRF4\11062002\J029221B.raw

3 <110> APPLICANT: Short, Jay M.  
4 Djavakhishvili, Tsotne David  
5 Frey, Gerhard Johann  
7 <120> TITLE OF INVENTION: Exonuclease-Mediated Nucleic Acid Reassembly in Directed  
Evolution  
9 <130> FILE REFERENCE: 112766.199  
11 <140> CURRENT APPLICATION NUMBER: US 10/029,221B  
C--> 12 <141> CURRENT FILING DATE: 2002-10-23  
14 <150> PRIOR APPLICATION NUMBER: US 60/008,311  
15 <151> PRIOR FILING DATE: 1995-12-07  
17 <150> PRIOR APPLICATION NUMBER: US 60/008,316  
18 <151> PRIOR FILING DATE: 1995-12-07  
20 <160> NUMBER OF SEQ ID NOS: 12  
22 <170> SOFTWARE: FastSEQ for Windows Version 4.0  
24 <210> SEQ ID NO: 1  
25 <211> LENGTH: 30  
26 <212> TYPE: DNA  
27 <213> ORGANISM: Artificial Sequence  
29 <220> FEATURE:  
30 <223> OTHER INFORMATION: defined sequence kernel  
-----  
W--> 32 <221> NAME/KEY: misc\_feature  
33 <222> LOCATION: 1, 2, 4, 5, 7, 8, 10, 11, 13, 14, 16, 17, 19, 20, 22, 23,  
34 25, 26, 28, 29  
35 <223> OTHER INFORMATION: n = A,T,C or G  
W--> 37 <400> 1  
W--> 38 nnknnknnkn nknnknnknn knnknnknnk 30  
40 <210> SEQ ID NO: 2  
41 <211> LENGTH: 30  
42 <212> TYPE: DNA  
43 <213> ORGANISM: Artificial Sequence  
45 <220> FEATURE:  
46 <223> OTHER INFORMATION: defined sequence kernel  
W--> 48 <221> NAME/KEY: misc\_feature  
49 <222> LOCATION: 1, 2, 4, 5, 7, 8, 10, 11, 13, 14, 16, 17, 19, 20, 22, 23,  
50 25, 26, 28, 29  
51 <223> OTHER INFORMATION: n = A,T,C or G  
W--> 53 <400> 2  
W--> 54 nnnnnnnnnnn nnnnnnnnnnn mnnnnnnnnnn 30  
56 <210> SEQ ID NO: 3  
57 <211> LENGTH: 5  
58 <212> TYPE: PRT  
59 <213> ORGANISM: Artificial Sequence  
61 <220> FEATURE:  
62 <223> OTHER INFORMATION: spacer peptide sequence of any number

## RAW SEQUENCE LISTING

PATENT APPLICATION: US/10/029,221B

DATE: 11/06/2002

TIME: 14:55:15

Input Set : A:\112766-199.ST25.txt

Output Set: N:\CRF4\11062002\J029221B.raw

64 <400> SEQUENCE: 3  
65 Gly Gly Gly Gly Ser  
66 1 5  
69 <210> SEQ ID NO: 4  
70 <211> LENGTH: 15  
71 <212> TYPE: PRT  
72 <213> ORGANISM: Artificial Sequence  
74 <220> FEATURE:  
75 <223> OTHER INFORMATION: linker peptide sequence  
77 <400> SEQUENCE: 4  
78 Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser  
79 1 5 10 15  
82 <210> SEQ ID NO: 5  
83 <211> LENGTH: 10  
84 <212> TYPE: DNA  
85 <213> ORGANISM: Artificial Sequence  
87 <220> FEATURE:  
88 <223> OTHER INFORMATION: primer  
90 <400> SEQUENCE: 5  
91 aaggaggag 10  
93 <210> SEQ ID NO: 6  
94 <211> LENGTH: 24  
95 <212> TYPE: DNA  
96 <213> ORGANISM: Artificial Sequence  
98 <220> FEATURE:  
99 <223> OTHER INFORMATION: forward primer  
W--> 101 <221> NAME/KEY: misc\_feature  
102 <222> LOCATION: 24  
103 <223> OTHER INFORMATION: n = A,T,C or G from 10 to 100  
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W--> 105 <400> 6  
W--> 106 ctagaagaga ggagaaaacc atgn 24  
108 <210> SEQ ID NO: 7  
109 <211> LENGTH: 22  
110 <212> TYPE: DNA  
111 <213> ORGANISM: Artificial Sequence  
113 <220> FEATURE:  
114 <223> OTHER INFORMATION: reverse primer  
W--> 116 <221> NAME/KEY: misc\_feature  
117 <222> LOCATION: 22  
118 <223> OTHER INFORMATION: n = A,T,C or G from 10 to 100  
W--> 120 <400> 7  
W--> 121 gatcaaaggc gcgcctgcag gn 22  
123 <210> SEQ ID NO: 8  
124 <211> LENGTH: 23  
125 <212> TYPE: DNA  
126 <213> ORGANISM: Artificial Sequence  
128 <220> FEATURE:  
129 <223> OTHER INFORMATION: forward primer  
131 <400> SEQUENCE: 8

## RAW SEQUENCE LISTING

PATENT APPLICATION: US/10/029,221B

DATE: 11/06/2002

TIME: 14:55:15

Input Set : A:\112766-199.ST25.txt

Output Set: N:\CRF4\11062002\J029221B.raw

132 ctagaaggga ggagaaaacc atg 23  
134 <210> SEQ ID NO: 9  
135 <211> LENGTH: 21  
136 <212> TYPE: DNA  
137 <213> ORGANISM: Artificial Sequence  
139 <220> FEATURE:  
140 <223> OTHER INFORMATION: reverse primer  
142 <400> SEQUENCE: 9  
143 gatcaaaggc ggcctgcag g 21  
145 <210> SEQ ID NO: 10  
146 <211> LENGTH: 43  
147 <212> TYPE: PRT  
148 <213> ORGANISM: Artificial Sequence  
150 <220> FEATURE:  
151 <223> OTHER INFORMATION: primer  
W--> 153 <221> NAME/KEY: VARIANT *also Xaa found at position 23*  
154 <222> LOCATION: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16,  
155 17, 18, 19, 20, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33,  
156 34, 35, 36, 37, 38, 39, 40, 41, 42, 43  
157 <223> OTHER INFORMATION: Xaa = Any Amino Acid  
W--> 159 <221> VARIANT  
160 <222> LOCATION: 23  
161 <223> OTHER INFORMATION: Xaa = Gly or Thr  
W--> 163 <400> 10  
W--> 164 Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa  
165 1 5 10 15  
W--> 166 Xaa Xaa Xaa Xaa Asn Asn Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa  
167 20 25 30  
W--> 168 Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa  
169 35 40

---

172 <210> SEQ ID NO: 11  
173 <211> LENGTH: 39  
174 <212> TYPE: DNA  
175 <213> ORGANISM: Artificial Sequence  
177 <220> FEATURE:  
178 <223> OTHER INFORMATION: forward primer  
180 <400> SEQUENCE: 11  
181 ctagaaggga ggagaattac atgaagcggc ttttagccc 39  
183 <210> SEQ ID NO: 12  
184 <211> LENGTH: 27  
185 <212> TYPE: DNA  
186 <213> ORGANISM: Artificial Sequence  
188 <220> FEATURE:  
189 <223> OTHER INFORMATION: reverse primer  
191 <400> SEQUENCE: 12  
192 agctaagggt caaggccgca cccgagg 27

RAW SEQUENCE LISTING ERROR SUMMARY  
PATENT APPLICATION: US/10/029,221B

DATE: 11/06/2002  
TIME: 14:55:16

Input Set : A:\112766-199.ST25.txt  
Output Set: N:\CRF4\11062002\J029221B.raw

Please Note:

Use of n and/or Xaa have been detected in the Sequence Listing. Please review the Sequence Listing to ensure that a corresponding explanation is presented in the <220> to <223> fields of each sequence which presents at least one n or Xaa.

Seq#:1; N Pos. 1,2,4,5,7,8,10,11,13,14,16,17,19,20,22,23,25,26,28,29  
Seq#:2; N Pos. 1,2,4,5,7,8,10,11,13,14,16,17,19,20,22,23,25,26,28,29  
Seq#:6; N Pos. 24  
Seq#:7; N Pos. 22  
Seq#:10; Xaa Pos. 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,23,24  
Seq#:10; Xaa Pos. 25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43



VERIFICATION SUMMARY

PATENT APPLICATION: US/10/029,221B

DATE: 11/06/2002

TIME: 14:55:16

Input Set : A:\112766-199.ST25.txt

Output Set: N:\CRF4\11062002\J029221B.raw

L:12 M:271 C: Current Filing Date differs, Replaced Current Filing Date  
 L:32 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!  
 L:37 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:1  
 L:38 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:1 after pos.:0  
 L:48 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!  
 L:53 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:2  
 L:54 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:2 after pos.:0  
 L:101 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!  
 L:105 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:6  
 L:106 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:6 after pos.:0  
 L:116 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!  
 L:120 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:7  
 L:121 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:7 after pos.:0  
 L:153 M:281 W: Numeric Fields not Ordered, <221> Sort in ascending order!  
 L:159 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:10  
 L:163 M:258 W: Mandatory Feature missing, <220> Tag not found for SEQ ID#:10  
 L:164 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:10 after pos.:0  
 L:166 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:10 after pos.:16  
 L:168 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:10 after pos.:32